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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,646	08/02/2001	Shinichi Ayabe	JKM-001	5225

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EXAMINER

KALLIS, RUSSELL

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 03/13/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/890,646

Applicant(s)

AYABE ET AL.

Examiner

Russell Kallis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 1,5,6,9-11,17,18,23 and 24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-4,7,8,12-16,19-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1 1/2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION***Election/Restrictions***

Applicant's election with traverse of Group II, claims 2-4, 7-8, 12-16, and 19-22 in Paper No. 8 is acknowledged. The traversal is on the ground(s) that there is unity among the restricted groups because the elucidation of the sense sequence automatically leads to the antisense DNA sequence and the protein encoded by the sense sequence, and that the cited reference to show that there is no special technical feature does not meet the limitations of the claim language when read in light of the specification. This is not found persuasive because the limitations of Claims 5-6 and 8-9 are broadly drawn to polynucleotides of unspecified coding sequences that can hybridize under mild or unspecified conditions to various parts or lengths of SEQ ID NO: 1. Further, Claim 3 recites the limitations "encodes 2-hydroxyisoflavone synthase or the nucleotide sequence complementary thereto". The limitation of a "nucleotide sequence complementary thereto" of a part of SEQ ID NO: 1 does not require that a 2-hydroxyisoflavone synthase be encoded, but only that the complementary sequence be taught and that is taught inherently.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

Claims 2, 12, and 22 are objected to because of the following informalities: Claims cannot depend from non-elected claims. Appropriate correction is required.



Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

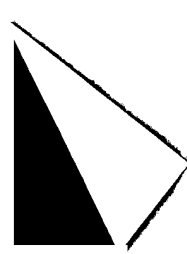
Claims 2-4, 7-8, 12-16, and 19-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims a polynucleotide “substantially comprising” a nucleotide sequence encoding a 2-hydroxyisoflavanonesynthase or a nucleotide sequence complementary thereto; a polynucleotide “substantially comprising” a nucleotide sequence having 50% sequence identity to SEQ ID NO: 1 encoding 2-hydroxyisoflavanone synthase or the nucleotide sequence complementary thereto; a polynucleotide sequence having 70% sequence identity to SEQ ID NO: 1 encoding a 2-hydroxyisoflavanone synthase, and polynucleotides that hybridize to SEQ ID NO: 1 under conditions of unspecified stringency.

Applicant describes SEQ ID NO: 1 encoding SEQ ID NO: 2.

Applicant does not describe any polynucleotides having more than 50% sequence identity to or hybridizing to SEQ ID NO: 1 and either encoding a 2-hydroxyisoflavanone synthase and/or a nucleotide sequence complementary thereto.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide an adequate written description of the claimed invention.



See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

Given the failure of the 2-hydroxyisoflavone synthase DNA or its variants to be adequately described, methods of its use are also inadequately described. See Written Description Guidelines, Federal Register Vol. 66 No. 4, Friday January 5, 2001 "Notices", pages 1099-1111.

Claims 2-4, 7-8, 12-16, and 19-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant broadly claims a polynucleotide "substantially comprising" a nucleotide sequence encoding a 2-hydroxyisoflavanonesynthase or a nucleotide sequence complementary thereto; a polynucleotide "substantially comprising" a nucleotide sequence having 50% sequence identity to SEQ ID NO: 1 encoding 2-hydroxyisoflavanone synthase or the nucleotide sequence

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complementary thereto; a polynucleotide sequence having 70% sequence identity to SEQ ID NO: 1 encoding a 2-hydroxyisoflavanone synthase; polynucleotides that hybridize to SEQ ID NO: 1 under conditions of unspecified stringency; and plant cells and plants comprising said sequences such that the products and derivatives thereof may be altered or increased.

Applicant teaches screening a cDNA library with a probe of 422 bp (SEQ ID NO: 3), a fragment of a gene of unspecified function, from *Glycyrrhiza echinata* (Example 2 pages 23-24); transformation and expression in yeast using an expression vector comprising SEQ ID NO: 1 (Example 3 pages 25-26); testing for active 2-hydroxyisoflavanone synthase activity in isolates from transformed yeast using a radiometric assay with radio-labeled liquiritigen and naringen (Example 4 pages 26-29); and transformation of tobacco with 2-hydroxyisoflavanone synthase cDNA (Example 7 pages 31-36).

Applicant does not teach isolation of any other sequences encoding a 2-hydroxyisoflavanone synthase other than SEQ ID NO: 1 or plants transformed with 2-hydroxyisoflavanone synthase other than tobacco transformed with SEQ ID NO: 1; or an altered phenotype in any plant transformed with a polynucleotide encoding a 2-hydroxyisoflavanone synthase.

Isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65⁰C (page 859, left column, 2nd paragraph). Fourgoux-Nicol et al also teach that the probe and

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isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2).

Further, the isolation of orthologous DNA sequences from other species introduces an element of unpredictability. The limitation is introduced in finding homologous regions that would adequately enable either PCR amplification or southern hybridization and would entail using either degenerate primers or probes with limited sequence identity. Thus the screen for orthologous sequences would isolate many genes other than those of interest. The inherent unpredictability in isolation of a homologous sequence encoding the same protein activity is illustrated in an example where a small number of changes to the coding region for a strict desaturase resulted in an enzyme with a hydroxylase activity and that a small number of changes to the coding region of a desaturase could account for the functional divergence seen across a range of enzymes involved in fatty acid metabolism (Broun P. *et al.* Science Vol. 282; 13 November 1998, pp. 1315-1317; Abstract lines 4-6 and p. 1317 column 1, lines 37-56).

Given the lack of guidance for isolating any other 2-hydroxyisoflavanone synthase genes, or for producing plants transformed with varied lengths of a 2-hydroxyisoflavanone synthase gene of SEQ ID NO: 1 in sense orientation or any other non-exemplified 2-hydroxyisoflavanone synthase genes in sense orientation, the breadth of the claims, and given the unpredictability in the art, undue trial and error experimentation would be needed by one skilled in the art to isolate a multitude of non-exemplified 2-hydroxyisoflavanone synthase genes, or to evaluate the ability

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of a multitude of non-exemplified 2-hydroxyisoflavanone synthase genes or non-exemplified gene fragments to alter the phenotype of a multitude of transformed plant species. Therefore, the invention is not enabled.

Claims 3, 4, 13-16 and 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

At Claim 3, line 2, "homology" is indefinite. It is unclear whether the term "homology" encompasses evolutionary derivations. The term "homology" should be replaced with --sequence identity--.

At Claim 4, line 1, "homology" is indefinite. It is unclear whether the term "homology" encompasses evolutionary derivations. The term "homology" should be replaced with --sequence identity--.

At Claim 4, lines 2-3, "a polynucleotide having a complementary sequence to the nucleotide sequences" is indefinite. It is unclear how the polynucleotide is to have a sequence complementary to a undefined number of various nucleotide sequences.

At Claim 4, line 2, before "2-hydroxyisoflavanone synthase" insert --a--.

At Claim 4, line 3, is very confusing. Delete line 3 and insert --complementary to said polynucleotide--.

At Claim 7, line 3, "conditions" should be plural.

At Claims 12, line 1, "A recombinant DNA or RNA containing an expression system" is recited as part of an expression system. RNA expression systems do not exist in the art and should be deleted from the claim.

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At Claims 13-14, line 1, "A recombinant DNA or RNA containing an expression system" is recited as part of an expression system. RNA expression systems do not exist in the art and should be deleted from the claim.

At Claim 13, line 2, "homology" is indefinite. It is unclear whether the term "homology" encompasses evolutionary derivations. The term "homology" should be replaced with --sequence identity--.

Claim 19 recites "A host cell containing one of the above mentioned recombinant DNAs or RNAs according to any one of Claims 12 to 16". Within the scope of the instant application and the scope of the claimed inventions of elected Group II, RNAs do not exist in host cells independently of the DNAs from which they are transcribed.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2-4 and 7-8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The DNA of Claims 2-4 and 7-8, since it has not been 'isolated' by the hand of man reads as a product of nature, thus falling outside the five classes of patentable subject matter.

The DNA molecule, as claimed, has the same characteristics and utility as those found naturally in the genome or as cellular precursors thereof and therefore does not constitute patentable subject matter. See *American Wood v. Fiber Distintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2-3, 7-8, 12, 14-16, and 19-20 are rejected under 35 U.S.C. 102(a) as being anticipated by Steele C. *et al.* Archives of Biochemistry and Biophysics; 1999, July 1; Vol. 367, No. 1; pp. 146-150 and GenBank accession number AF135484 submitted March 17, 1999; see result 7 of sequence report.

The claims are broadly drawn to a polynucleotide having more than 50% sequence identity to SEQ ID NO: 1 encoding a 2-hydroxyisoflavanone synthase and expression of said polynucleotide in a host cultured cell.

Steele teaches a polynucleotide (CYP93C1) encoding a 2-hydroxyisoflavanone synthase having more than 50% sequence identity (homology) to SEQ ID NO: 1 and cloning of said sequence into a baculovirus vector for functional identification when expressed in cultured insect cells (page 147 column 1, 2nd full paragraph to page 148 column 2, end of 1st paragraph).

Thus, the reference teaches all the limitations of Claims 2-3, 7-8, 12, 14-16, and 19-21.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

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Claims 2-3 and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Siminszky B. *et al.* GenBank Accession number AF022462 submitted on September 4, 1997; see result 8 of sequence report; in light of Steele *et al.* (1999).

The claims are broadly drawn to a polynucleotide substantially comprising a nucleotide sequence encoding the 2-hydroxyisoflavone synthase of SEQ ID NO: 2 or having 50% sequence identity to SEQ ID NO: 1 and that encodes 2-hydroxyisoflavone synthase, or a nucleotide sequence complementary thereto.

Siminszky teaches the coding region, with greater than 50% homology to SEQ ID NO: 1, which encodes a CYP93C1 class cytochrome P450, in light of the teachings of Steele *et al.* cited above.

Thus, the reference teaches all the limitations of Claims 2-3 and 7-8.

Claims 2-3 and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Akashi T. *et al.* GenBank Accession number D89436, submitted on November 20, 1996; see result 2 of sequence report.

Claims 2-3 recite “substantially comprising” as defined in the specification on page 4 lines 8-15 (special consideration is directed to “and encodes IFS or the nucleotide sequence complementary thereto”) and are broadly drawn to any part of SEQ ID NO: 1 of unspecified length having 50% sequence identity to the unspecified part of SEQ ID NO: 1. Claim 7 broadly recites a polynucleotide, which hybridizes under conditions of unspecified stringency, including mild stringency, to a portion of SEQ ID NO: 1. Claim 8 broadly recites a polynucleotide which can be hybridized to SEQ ID NO: 1 under mild conditions.

Akashi teaches a fragment of 202 nucleotides of a cytochrome P450 gene having 100% sequence identity to nucleotides 1521 to 1733 of SEQ ID NO: 1.

Thus, the reference teaches all the limitations of Claims 2-3 and 7-8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Steele C. *et al.* alone; Archives of Biochemistry and Biophysics; 1999, July 1; Vol. 367, No. 1; pp. 146-150 in light of GenBank accession number AF135484 submitted March 17, 1999; see result 7 of sequence report and whereby the methods of culturing and collecting recombinant 2-hydroxyisoflavanone synthase would be an obvious design choice given the general and well known utility of baculovirus expression vectors transformed into insect cells for expressing recombinant proteins at levels convenient for isolation.

Applicant broadly claims a method for producing 2-hydroxyisoflavone synthase comprising a step of collecting the produced recombinant enzyme.

The teachings of Steele are discussed *supra*.

It would have been obvious at the time of Applicant's invention to modify the invention of Steele to incorporate a method of culturing and collecting recombinant 2-hydroxyisoflavanone synthase from transformed insect cells. One of skill in the art would have been motivated by the knowledge common in the art that recombinant proteins are valuable materials for scientific and

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commercial products, and that one would have had a reasonable expectation of success of expressing genes in transformed insect cells given the common and successful usage of the baculovirus expression vectors.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Napoli C. *et al.* Plant Cell; April 1990; Vol. 2; pp. 279-289 in view of Steele C. *et al.* Archives of Biochemistry and Biophysics; 1999, July 1; Vol. 367, No. 1; pp. 146-150 in light of GenBank accession number AF135484 submitted March 17, 1999; see result 7 of sequence report.

Applicant broadly claims a transgenic plant having altered or increased product or derivative of 2-hydroxyisoflavanone synthase by transformation with a recombinant DNA or RNA having 70% or more homology (sequence identity) to nucleotide sequence 144-1712 of SEQ ID NO: 1 or that can be hybridized to nucleotide sequence 144- 1712 of SEQ ID NO: 1.

Napoli teaches alteration of the flavanoid pathway by co-suppression of chalcone synthase in petunia by overexpression of a chimeric chalcone synthase gene (page 279, Abstract and page 283, discussion of Figure 4 from column 1 to column 2).

Napoli does not teach a gene encoding a 2-hydroxyisoflavanone synthase.

The teachings of Steele are discussed supra.

It would have been obvious at the time of Applicant's invention to modify the invention of Napoli teaching alteration in products or derivatives of the chalcone synthase gene by overexpressing a recombinant chalcone synthase gene to substitute a cDNA encoding the 2-isohydroxyflavanone synthase gene taught by Steele into the recombinant expression vector. One of skill in the art would have been motivated by the success of Napoli in altering a component of flavonoid biosynthesis by overexpressing one of the genes of the biosynthetic pathway and by

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the suggestion of plant transformation by Steele *et al.* on p. 149, column 2, bottom paragraph; and that one would have had a reasonable expectation of success of expressing flavonoid biosynthetic genes in transformed plants.

All Claims are rejected.

Claims 4 and 13 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide having 70% or more sequence identity to SEQ ID NO: 1.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding, or if the examiner cannot be reached as indicated above, should be directed to the receptionist, whose telephone number is (703) 308-0196.

Russell Kallis Ph.D.
March 3, 2003

DAVID T. FOX
PRIMARY EXAMINER
GROUP 188-1638

